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=> dup rem l39 l43
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PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L43
L44           34 DUP REM L39 L43 (19 DUPLICATES REMOVED)
                 ANSWERS '1-21' FROM FILE HCAPLUS
                 ANSWER '22' FROM FILE MEDLINE
                 ANSWER '23' FROM FILE EMBASE
                 ANSWERS '24-26' FROM FILE BIOSIS
                 ANSWERS '27-34' FROM FILE WPIX

=> d que
L37           91 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GENE?/CT(L)(YGBB OR YFHC OR
                 YACE OR YCHB OR YEJD OR YRFL OR YGGJ OR YJEE OR YIAO OR YRDC
                 OR YHBC OR YGBP OR YBEY OR GCPE OR KDTB OR PFS OR YCAJ OR
                 B1808 OR YEAA OR YAGF OR B1983 OR YIDD OR YCEG OR YJBC)
L38           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L37 AND (ANTAG? OR INHIB? OR
                 BLOCK?)
L39           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 AND (BACTER? OR ANTIBACTER
                 ? OR MICROB? OR ANTIMICROB?)
L40         3192 SEA (YGBB OR YFHC OR YACE OR YCHB OR YEJD OR YRFL OR YGGJ OR
                 YJEE OR YIAO OR YRDC OR YHBC OR YGBP OR YBEY OR GCPE OR KDTB
                 OR PFS OR YCAJ OR B1808 OR YEAA OR YAGF OR B1983 OR YIDD OR
                 YCEG OR YJBC)
L41          390 SEA L40 AND GENE
L42          148 SEA L41 AND (BACTER? OR ANTIBACTER?)
L43           32 SEA L42 AND (ANTAG? OR INHIB? OR BLOCK?)
L44           34 DUP REM L39 L43 (19 DUPLICATES REMOVED)


=> d l44 bib ab 1-34

L44  ANSWER 1 OF 34  HCAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN   2004:3019  HCAPLUS
DN   140:70982
TI   Methods for identifying antimicrobial agents inhibiting
     bacterial tRNA:34A deaminase gene yfhC, and related antisense
     oligonucleotides targeted to anticodon stem loop of tRNAArg(ACG)
IN   Pollard, Mike G.; Cota, Adam; Hoeppner, Corey; Mehlhorn, Ingrid E.; Cole,
     Timothy David; Neiman, Joshua Alan; Roberts, Guy T.; Mitchell, Wayne
PA   Tao Biosciences, LLC, USA
SO   PCT Int. Appl., 56 pp.
     CODEN: PIXXD2
DT   Patent
```

LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004001017	A2	20031231	WO 2003-US20265	20030625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2002-183923	A	20020625
	US 2002-184503	A	20020626
	US 2002-396535P	P	20020715

AB The invention provides methods of identifying compds. that **inhibit** specific tRNA:34A deaminases encoded by yfhC genes, compds. that **inhibit** such deaminases and methods of using the deaminases in a variety of in vitro and in vivo contexts, such as in the treatment and prevention of **bacterial** infections. Specifically disclosed are sequences of gene yfhC and its encoded tRNA:34A deaminase from E. coli strain K-12 (EcoGene accession number EG1 1372, or P30134 or GenBank accession number AE000342/ACC75612). This E. coli yfhC deaminase is demonstrated to catalyze the formation of inosine 34 in the anticodon of tRNA using a truncated substrate corresponding to anticodon stem loop of tRNAArg(ACG). A series of tRNAArg(ACG) of various different **bacterial** species are also provided, which can be useful targets for antisense oligonucleotides for the identification **antimicrobial** agents.

L44 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
AN 2002:793769 HCAPLUS
DN 137:305787
TI Streptococcus pneumoniae yacM and yqeJ essential genes and proteins, orthologs and homologs thereof, and their use in identifying **antibacterial** agents
IN Fritz, Christian; Youngman, Philip; Guzman, Luz-Maria
PA Millennium Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002081652	A2	20021017	WO 2002-US5086	20020221
WO 2002081652	A3	20031218		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2002160364	A1	20021031	US 2001-792251	20010223
	US 6664074	B2	20031216		
PRAI	US 2001-792251	A1	20010223		

AB The invention is based on the discovery that the yacM and yqeJ genes of the Gram pos. **bacterium** Streptococcus pneumoniae, are essential for survival. Identification of these genes allows homologs of the essential genes to be found in other strains within the species, and orthologs of the essential genes to be found in other organisms (e.g., Bacillus subtilis and Escherichia coli). These genes and the essential polypeptides they encode can be used to identify **antibacterial** agents for treating a broad spectrum of **bacterial** infections. Such agents can **inhibit bacterial** growth by **inhibiting** the activity of an essential protein, or by **inhibiting** transcription of an essential gene or translation of the mRNA transcribed from the essential gene.

L44 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
AN 2002:123201 HCAPLUS
DN 136:162385
TI Methyl-D-erythritol phosphate pathway gene gcpE from Arabidopsis thaliana and other plants
IN Boronat, Albert; Campos, Narciso; Rodriguez-Concepcion, Manuel; Rohmer, Michel; Seeman, Myriam; Valentin, Henry E.; Venkatesh, Tyamagondlu V.; Venkatramesh, Mylavarapu
PA Monsanto Technology, LLC, USA
SO PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002012478	A2	20020214	WO 2001-US24335	20010806
	WO 2002012478	C1	20020704		
	WO 2002012478	A3	20030703		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2001090522	A5	20020218	AU 2001-90522	20010806
	US 2002069426	A1	20020606	US 2001-921992	20010806
	EP 1356033	A2	20031029	EP 2001-970529	20010806

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI	US 2000-223483P	P	20000807
	WO 2001-US24335	W	20010806

AB The present invention provides and includes nucleic acids, proteins and antibodies associated with novel genes in the methyl-D-erythritol phosphate (MEP) biosynthesis pathway. Specifically, a homolog of the Escherichia coli gcpE gene is found in Arabidopsis thaliana which catalyzes the conversion of 2-C-methyl-D-erythritol 2,4-cyclodiphophate to (E)-1-(4-hydroxy-3-methylbut-2-enyl) diphosphate. Partial gene sequences

are also provided from soybean, tomato, Mesembryanthemum crystallinum, rice, maize, loblolly pine, soybean, Brassica, and Physcomitrella patens. The invention further encompasses methods utilizing such mols., for example in gene isolation, gene anal. and the production of transgenic plants. The present invention also includes transgenic plants modified to express proteins associated with the MEP pathway. Modulation of isoprenoid, tocopherol, monoterpene, and carotenoid levels can be achieved in transgenic plants.

L44 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
AN 2002:478819 HCAPLUS
DN 137:198023
TI pfs-Dependent regulation of autoinducer 2 production in Salmonella enterica serovar typhimurium
AU Beeston, Anne L.; Surette, Michael G.
CS Department of Microbiology and Infectious Diseases, University of Calgary, Calgary, AB, T2N 4N1, Can.
SO Journal of Bacteriology (2002), 184(13), 3450-3456
CODEN: JOBAAY; ISSN: 0021-9193
PB American Society for Microbiology
DT Journal
LA English
AB **Bacterial** intercellular communication provides a mechanism for signal-dependent regulation of gene expression to promote coordinated population behavior. S. enterica typhimurium produces a non-homoserine lactone autoinducer in exponential phase as detected by a Vibrio harveyi reporter assay for autoinducer 2 (AI-2). The luxS gene product mediates the production of AI-2. Environmental cues such as rapid growth, the presence of preferred C sources, low pH, and/or high osmolarity were found to influence the production of AI-2. In addition to LuxS, the pfs gene product (Pfs) is required for AI-2 production, as well as S-adenosylhomocysteine (SAH). In **bacterial** cells, Pfs exhibits both 5'-methylthioadenosine (MTA) and SAH nucleosidase functions. Pfs is involved in methionine metabolism, regulating intracellular MTA and SAH levels (elevated levels of MTA and SAH are potent **inhibitors** of polyamine synthetases and S-adenosylmethionine dependent methyltransferase reactions, resp.). To further investigate regulation of AI-2 production in Salmonella, we constructed pfs and luxS promoter fusions to a luxCDABE reporter in a low-copy-number vector, allowing an examination of transcription of the genes in the pathway for signal synthesis. Here we report that luxS expression is constitutive but that the transcription of pfs is tightly correlated to AI-2 production in Salmonella serovar Typhimurium 14028. Neither luxS nor pfs expression appears to be regulated by AI-2. These results suggest that AI-2 production is regulated at the level of LuxS substrate availability and not at the level of luxS expression. Our results indicate that AI-2-dependent signaling is a reflection of metabolic state of the cell and not cell d.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
AN 2001:115301 HCAPLUS
DN 134:188989
TI Metabolic pathways and enzymes in isoprenoid biosynthesis and their use in screening assays for **inhibitors** and herbicide resistance
IN Bacher, Adelbert; Zenk, Meinhart; Eisenreich, Wolfgang; Fellermeier, Monika; Fischer, Markus; Hecht, Stefan; Herz, Stefan; Kis, Klaus; Luttgen, Holger; Rohdich, Felix; Sagner, Silvia; Schuhr, Christoph A.;

Wungsintaweekul, Juraithip
PA Germany
SO PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001011055	A1	20010215	WO 2000-EP7548	20000803
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 10020996	A1	20010322	DE 2000-10020996	20000428
	EP 1198575	A1	20020424	EP 2000-949452	20000803
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRAI	DE 1999-19936663	A	19990804
	DE 1999-19945174	A	19990921
	DE 1999-19945175	A	19990921
	DE 1999-19948887	A	19991011
	DE 1999-19953309	A	19991105
	DE 2000-10020996	A	20000428
	WO 2000-EP7548	W	20000803

AB The present invention relates to enzymic activity involved in isoprenoid biosynthesis as well as to **inhibitors**, notably herbicides, for enzymes in the biosynthesis of isoprenoids. More specifically, the present invention relates to screening methods for detecting such **inhibitors**, and to enzymically active proteins for performing said methods as well as purified isolated DNA coding for such proteins. Moreover, the present invention relates to novel **inhibitors** detectable by said screening methods as well as compns. and processes for **inhibiting** the synthesis of isoprenoids and for controlling the growth of organisms based on said **inhibitors**. The invention relates also to the development of **inhibitor**-resistant plant enzymes and plants, plant tissues, plant seeds and plant cells. Thus, isoprenoid biosynthesis is shown to proceed via: (1) 2C-methyl-D-erythritol 4-phosphate plus CTP conversion to 4-diphosphocytidyl 2C-methyl-D-erythritol (I) as catalyzed by 4-diphosphocytidyl-2C-methyl-D-erythritol synthase; (2) I plus ATP conversion to 4-diphosphocytidy-2C-methyl-D-erythritol 2-phosphate (II) via 4-diphosphocytidyl-2C-methyl-D-erythritol kinase; and (3) followed by conversion of II to 2C-methyl-D-erythritol 2,4-cyclopyrophosphate via 2C-Methyl-D-erythritol 2,4-cyclodiphosphate synthase. Genes ygbP, ychB, and ygbB encoding these enzymes are cloned from Escherichia coli, Arabidopsis thaliana, and tomato. The enzymes provide applications in screening for herbicidal **inhibitors** and for genetic engineering of herbicide resistance in plants.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
AN 2001:885255 HCAPLUS

DN 136:34648
TI Genes, enzymes, labeled intermediates, and methods for analysis of mevalonate-independent isoprenoid biosynthesis pathway
IN Adam, Petra; Bacher, Adelbert; Eisenreich, Wolfgang; Fellermeier, Monika; Hecht, Stefan; Rohdich, Felix; Schuhr, Christoph A.; Wungsintaweekul, Juraithip; Zenk, Meinhart H.
PA Germany
SO Ger. Offen., 38 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10027821	A1	20011206	DE 2000-10027821	20000605
	WO 2001094561	A2	20011213	WO 2001-EP6255	20010601
	WO 2001094561	A3	20020530		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1287145	A2	20030305	EP 2001-940547	20010601
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004072142	A1	20040415	US 2003-296416	20030708
PRAI	DE 2000-10027821	A	20000605		
	WO 2001-EP6255	W	20010601		

AB The present invention concerns enzymes and intermediates of the mevalonate-independent isoprenoid biosynthesis pathway downstream from 2C-methyl-D-erythritol-2,4-cyclopyrophosphate and upstream from isopentenylpyrophosphate or dimethylallylpyrophosphate. These are used for screening for **inhibitors** of these enzymes and for identification of **inhibitor**-resistant variants. Further disclosures concern genes coding for the enzymes and for **inhibitor** -resistant variants of the enzymes, vectors which contain the genes, cells which contain the vectors, and plant seeds containing such vectors. Thus, the Bacillus subtilis and Escherichia coli genes for the mevalonate-independent isoprenoid biosynthesis pathway were cloned and expressed. The DXP synthase and DXP reductoisomerase enzymes were used to prepare [U-13C5]-2C-methyl-D-erythritol-4-phosphate. The gene yqiE 1-deoxy-D-xylulose-5-phosphate synthase, gene yaeM 1-deoxy-D-xylulose-5-phosphate reductoisomerase, and gene ygbP 4-diphosphocytidyl-2C-methyl-D-erythritol synthase were used in preparation of [2,2-13C2]-4-diphosphocytidyl-2C-methyl-D-erythritol. Genes downstream of ygbP, i.e., gcpE, lytB, yjeE, and ybeB were cloned for use in screening for **inhibitors** of isoprenoid biosynthesis or for preparing intermediates in the pathway.

L44 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
AN 2001:348500 HCAPLUS
DN 135:104920
TI Identification of novel essential Escherichia coli genes conserved among pathogenic **bacteria**
AU Freiberg, Christoph; Wieland, Bernd; Spaltmann, Frank; Ehlert, Kerstin; Brotz, Heike; Labischinski, Harald

CS Pharma Research, Bayer AG, Institute for Anti-infectives Research, Wuppertal, D-42096, Germany
SO Journal of Molecular Microbiology and Biotechnology (2001), 3(3), 483-489
CODEN: JMMBFF; ISSN: 1464-1801
PB Horizon Scientific Press
DT Journal
LA English
AB We deleted a subset of 27 open reading frames (ORFs) from Escherichia coli which encode previously uncharacterized, probably soluble gene products homologous to proteins from a broad spectrum of **bacterial** pathogens such as Haemophilus influenzae, Staphylococcus aureus, Streptococcus pneumoniae and Enterococcus faecalis and only distantly related to eukaryotic proteins. Six novel **bacteria**-specific genes essential for growth in complex medium could be identified through a combination of bioinformatics-based and exptl. approaches. We also compared our data to published results of gene inactivation projects with Mycoplasma genitalium and Bacillus subtilis and looked for homologs in all known prokaryotic genomes. Such analyses highlight the enormous metabolic flexibility of prokaryotes. Six of 27 studied genes have been functionally characterized up to now, amongst these four of the essential genes. The gene products YgbP, YgbB and YchB are involved in the non-mevalonate pathway of isoprenoid biosynthesis. KdtB is characterized as the phosphopantetheine adenylyltransferase CoaD. There are indications that the other two essential gene products YjeE and YqgF, which we have identified, also possess enzymic functions. These findings demonstrate the potential of such proteins to be used in screening of large chemical libraries for **inhibitors** which could be further developed to novel broad-spectrum antibiotics.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
AN 2001:77831 HCAPLUS
DN 135:164538
TI Escherichia coli engineered to synthesize isopentenyl diphosphate and dimethylallyl diphosphate from mevalonate: a novel system for the genetic analysis of the 2-C-methyl-D-erythritol 4-phosphate pathway for isoprenoid biosynthesis
AU Campos, Narciso; Rodriguez-Concepcion, Manuel; Sauret-Gueto, Susanna; Gallego, Francesca; Lois, Luisa-Maria; Boronat, Albert
CS Department de Bioquimica i Biologia Molecular, Facultat de Quimica, Universitat de Barcelona, Barcelona, 08028, Spain
SO Biochemical Journal (2001), 353(1), 59-67
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
AB Isopentenyl diphosphate (IPP) and its isomer dimethylallyl diphosphate (DMAPP) constitute the basic building **block** of isoprenoids, a family of compds. that is extraordinarily diverse in structure and function. IPP and DMAPP can be synthesized by two independent pathways: the mevalonate pathway and the recently discovered 2-C-methyl-D-erythritol 4-phosphate (MEP) pathway. Although the MEP pathway is essential in most eubacteria, algae and plants and has enormous biotechnol. interest, only some of its steps have been determined We devised a system suitable for the genetic anal. of the MEP pathway in Escherichia coli. A synthetic operon coding for yeast 5-diphosphomevalonate decarboxylase, human 5-phosphomevalonate kinase, yeast mevalonate kinase and E. coli isopentenyl diphosphate isomerase was incorporated in the chromosome of

this **bacterium**. The expression of this operon allowed the synthesis of IPP and DMAPP from mevalonate added exogenously and complementation of lethal mutants of the MEP pathway. We used this system to show that the ygbP, ychB and ygbB genes are essential in E. coli and that the steps catalyzed by the products of these genes belong to the trunk line of the MEP pathway.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
AN 2000:742284 HCAPLUS
DN 133:317528
TI Novel method for identifying **antibacterial** compounds
IN Loferer, Hannes; Jacobi, Alexander
PA GPC Biotech A.-G., Germany
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000061793	A2	20001019	WO 2000-EP3135	20000407
	WO 2000061793	A3	20010111		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1043403	A1	20001011	EP 1999-107031	19990409
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EP 1165832	A2	20020102	EP 2000-920677	20000407
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002541820	T2	20021210	JP 2000-611715	20000407
	US 2004086937	A1	20040506	US 2001-973674	20011009
PRAI	EP 1999-107031	A	19990409		
	EP 2000-102111	A	20000204		
	WO 2000-EP3135	W	20000407		

AB The present invention relates to a method for identifying an **antagonist** or **inhibitor** of the expression of a gene encoding a polypeptide essential for **bacterial** growth or survival as well as for an **antagonist** or **inhibitor** of said polypeptide. The invention further relates to a method for improving **antagonists** or **inhibitors**. The invention also provides an **antagonist** or **inhibitor** of the activity of said polypeptide. The invention is further related to a method for producing a therapeutic agent in a composition comprising said **antagonist** or **inhibitor**. Furthermore, the invention is related to the use of the polypeptide and the **antagonist** or **inhibitor** as well as to a method to identify a surrogate marker.

L44 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 11
AN 2000:210210 HCAPLUS

DN 132:247171
TI Genes of deoxyxylulose biosynthetic pathway, their expression in plants, and their use in screening for **antimicrobials**
IN Jomaa, Hassan
PA Germany
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000017233	A2	20000330	WO 1999-EP7055	19990922
	WO 2000017233	A3	20000525		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19923567	A1	20000406	DE 1999-19923567	19990521
	CA 2334645	AA	19991229	CA 1999-2334645	19990623
	EP 1100510	A2	20010523	EP 1999-929309	19990623
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	JP 2002518418	T2	20020625	JP 2000-555562	19990623
	AU 752714	B2	20020926	AU 1999-46155	19990623
	AU 9946155	A1	20000110		
	CA 2343919	AA	20000330	CA 1999-2343919	19990922
	AU 9961947	A1	20000410	AU 1999-61947	19990922
	AU 767213	B2	20031106		
	BR 9914028	A	20010703	BR 1999-14028	19990922
	EP 1115849	A2	20010718	EP 1999-948831	19990922
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200100836	T2	20011022	TR 2001-20010083619990922	
	EE 200100174	A	20020815	EE 2001-174	19990922
	JP 2002526061	T2	20020820	JP 2000-574141	19990922
	ZA 2001001913	A	20020307	ZA 2001-1913	20010307
	BG 105361	A	20011031	BG 2001-105361	20010319
	HR 2001000215	A1	20020630	HR 2001-215	20010321
	NO 2001001459	A	20010522	NO 2001-1459	20010322
PRAI	DE 1998-19843279	A	19980922		
	DE 1999-19923567	A	19990521		
	DE 1998-19828097	A	19980624		
	WO 1999-EP4360	W	19990623		
	WO 1999-EP7055	W	19990922		

AB The invention relates to the 1-deoxy- D-xylulose-5-phosphate reductoisomerase gene, the 1-deoxy-D-xylulose-5-phosphate synthase gene, and the gcpE gene of the 1-deoxy-D-xylulose biosynthetic pathway and to their use in transforming vectors, host organisms, and plants, and for determining substances that **inhibit** this biosynthetic pathway. Thus, the genes for D-xylulose-5-phosphate reductoisomerase and 1-deoxy-D-xylulose-5-phosphate synthase and the gcpE gene of Plasmodium falciparum were cloned and sequenced.

L44 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 12
AN 2000:723209 HCAPLUS
DN 133:291082
TI Gene expression **inhibition** method for screening **antibacterial** compounds
PA GPC A.-G., Genome Pharmaceuticals Corporation, Germany
SO Eur. Pat. Appl., 55 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1043403	A1	20001011	EP 1999-107031	19990409
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 2000061793	A2	20001019	WO 2000-EP3135	20000407
	WO 2000061793	A3	20010111		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1165832	A2	20020102	EP 2000-920677	20000407
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002541820	T2	20021210	JP 2000-611715	20000407
	US 2004086937	A1	20040506	US 2001-973674	20011009
PRAI	EP 1999-107031	A	19990409		
	EP 2000-102111	A	20000204		
	WO 2000-EP3135	W	20000407		

AB The present invention relates to a method for identifying an **antagonist** or **inhibitor** of the expression of a gene encoding a polypeptide essential for **bacterial** growth or survival as well as for an **antagonist** or **inhibitor** of said polypeptide. The invention further relates to a method for improved **antagonists** or **inhibitors**. The invention also provides an **antagonist** or **inhibitor** of the activity of said polypeptide. The invention is further related to a method for producing a therapeutic agent in a composition comprising said **antagonist** or **inhibitor**. Furthermore, the invention is related to the use of the polypeptide and the **antagonist** or **inhibitor** as well as to a method to identify a surrogate marker.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:355103 HCAPLUS
DN 140:370805
TI Colorimetric assays for the enzymatic activity of LytB and GcpE gene products involved in the alternate pathway of mevalonate biosynthesis
IN Altincicek, Boran; Hintz, Martin; Jomaa, Hassan; Kollas, Ann-kristin; Sanderbrand, Silke; Wiesner, Jochen
PA Bioagency A.-G., Germany
SO PCT Int. Appl., 16 pp.

CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004035810	A2	20040429	WO 2003-EP10900	20031002

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DE 2002-10247478 A 20021011

AB The invention relates to a method for determining the enzymic activity of GcpE and LytB proteins, in particular to the use of an electron carrier like dithionite, Me viologen, benzyl viologen or an appropriated protein for measuring a substrate reaction by photometry. The inventive method is used for identifying the **inhibitors** of an enzymic activity of the GcpE and LytB proteins in the form of **antibacterial**, antiparasitic agents and pesticides or in the form of conductivity structures for developing similar type active agents.

L44 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:201395 HCAPLUS
DN 140:248119
TI Genome-wide gene expression analysis with DNA chips for the characterization of glucose-overflow metabolism in Escherichia coli
AU Polen, Tino
CS Germany
SO Schriften des Forschungszentrums Juelich, Lebenswissenschaften/Life Sciences (2003), 5, a, 1-101
CODEN: SFLSF9; ISSN: 1433-5549
PB Forschungszentrum Juelich GmbH
DT Journal
LA German

AB In the present work differentially expressed genes of Escherichia coli MG1655 as a consequence of (i) acetate metabolism due to growth on acetate as sole carbon and energy source, (ii) a toxic acetate effect due to the presence of acetate in complex media and (iii) the aerobic acetate formation in glucose overflow metabolism were identified by genome-wide gene expression anal. using DNA microarrays. After successfully establishing DNA microarray technol. at the institute, the known regulation phenomena in E. coli MG1655 during growth on fructose, lactate, pyruvate or glycerin were characterized on the genome level. The specific genome-wide gene expression changes due to growth on acetate or propionate were determined In the presence of 20 mM acetate or 20 mM propionate growth of E. coli on complex media was only slightly **inhibited**. Under these conditions mainly three sets of differentially expressed genes were identified:. Chemotaxis and flagella genes (i),. Genes of the general stress response (ii) and. Genes for uptake and utilization of carbon and energy sources others than glucose (iii). Increased expression of chemotaxis and flagella genes was shown to result in increased motility on

the phenotypic level in the presence of 20 mM acetate or 20 mM propionate. Using continuous aerobic cultures of E. coli MG1655 increased aerobic acetate formation was shown to correlate with increased glucose feed only in a small concentration range. In that range an increase of glucose feed by only 1.7 mM results in the maximally observed specific aerobic acetate formation rate of 10 mmol/g/h. DNA microarray anal. of these cultures revealed decreased expression of genes encoding enzymes of the tricarboxylic acid cycle, the glyoxylate bypass and the NADH dehydrogenase I of the respiratory chain. The resulting diminished acetyl-CoA oxidizing capacity of the TCA-cycle accounts for the aerobic acetate formation under these conditions.

RE.CNT 139 THERE ARE 139 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:814359 HCAPLUS
DN 137:321247
TI Screening method for anti-**microbial** drug targets by genome-saturating mutagenesis (GSM) using a conditionally replicating vector
IN Fuchs, Thilo M.
PA Creatogen Aktiengesellschaft, Germany
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002083940	A2	20021024	WO 2002-EP3874	20020408
	WO 2002083940	A3	20040219		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	EP 2001-108774	A	20010406
	EP 2001-110443	A	20010427
	EP 2001-120181	A	20010822

AB This invention relates to a novel method for the identification of obligatory essential nucleic acid sequences, in particular **microbial** sequences. If a genome-representing nucleic acid sequence library of a microorganism of interest (also called fragment library) is established in a conditionally replicating vector, the method may comprise a genome saturating mutagenesis. An important feature of genome saturating mutagenesis according to the invention is that those genomic fragments which are identified and further investigated contain an obligatory essential nucleic acid sequence. This is an advantage in comparison to a "neg." approach like transposon-mutagenesis that identifies only gene loci which can be disrupted by insertional mutagenesis without loss of cell viability. Moreover, since every ORF in an operon will be mutagenized, polar effects can be studied rapidly, instead of analyzing an operon by time-consuming subsequent knock out steps. The invention can be applied to any microorganism of interest.

Obligatory essential genes of Salmonella enterica typhimurium were identified using the method of invention. Further, a method for the identification of novel **antimicrobial** compds. using the obligatory essential nucleic acids and proteins encoded thereby is provided.

L44 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:792042 HCAPLUS
DN 137:306627
TI Enzymes and intermediates of mevalonate-independent isoprenoid biosynthesis and the development of antibiotics
IN Adam, Petra; Amsingler, Sabine; Bacher, Adelbert; Eisenreich, Wolfgang; Hecht, Stefan; Rohdich, Felix
PA Germany
SO Ger. Offen., 78 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10201458	A1	20021017	DE 2002-10201458	20020116
WO 2002083720	A2	20021024	WO 2002-EP4005	20020410
WO 2002083720	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1377663	A2	20040107	EP 2002-724284	20020410

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI	DE 2001-10118166	A1	20010411
	DE 2001-10130236	A1	20010622
	DE 2001-10155084	A1	20011109
	DE 2002-10201458	A	20020116
	WO 2002-EP4005	W	20020410

OS MARPAT 137:306627
AB A biosynthetic pathway for isoprenoids that uses 1-deoxy-D-xylulose-5-phosphate (I) as a key intermediate rather than mevalonic acid as an intermediate is described. This pathway is used by a number of pathogens with one of the key intermediates, 1-hydroxy-2-methyl-2-butenyl-4-diphosphate (II), stimulating γδT cells. The pathway may therefore be useful in the diagnosis of infection and development of antibiotics. Genes for the enzymes of the pathway are cloned and expressed for use in the development of antibiotics **inhibiting** the pathway. The invention provides furthermore II, a new intermediate in the mevalonate-independent isoprenoid biosynthetic pathway downstream from 2C-methyl-D-erythritol-2,4-cyclodiphosphate. The metabolism of 13C-labeled I was studied in Escherichia coli. A major sink for I was II with several labeled intermediates also identified. The structure of the novel intermediates was confirmed by synthesis.

L44 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:715769 HCAPLUS
DN 138:20341
TI Antibiotics that **inhibit** cell wall biosynthesis induce expression of the Bacillus subtilis σW and σM regulons
AU Cao, Min; Wang, Tao; Ye, Rick; Helmann, John D.
CS Department of Microbiology, Cornell University, Ithaca, NY, 14853-8101, USA
SO Molecular Microbiology (2002), 45(5), 1267-1276
CODEN: MOMIEE; ISSN: 0950-382X
PB Blackwell Science Ltd.
DT Journal
LA English
AB Bacillus subtilis encodes seven extracytoplasmic function (ECF) sigma factors. The σW regulon includes functions involved in detoxification and protection against **antimicrobials**, whereas σM is essential for growth at high salt concns. We now report that antibiotics that **inhibit** cell wall biosynthesis induce both σW and σM regulons as monitored using DNA microarrays. Induction of selected σW-dependent genes was confirmed using lacZ reporter fusions and Northern blot anal. The ability of vancomycin to induce the σW regulon is dependent on both σW and the cognate anti-σ, RsiW, but is independent of the transition state regulator AbrB. These results suggest that the membrane-localized RsiW anti-σW factor mediates the transcriptional response to cell wall stress. Our findings are consistent with the idea that one function of ECF σ factors is to coordinate antibiosis stress responses and cell envelope homeostasis.
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:816926 HCAPLUS
DN 135:354706
TI Structure of diphosphocytidyl methylerythritol synthetase involved in mevalonate-independent isoprenoid biosynthesis and the rational design of effectors
IN Noel, Joseph P.; Bowman, Marianne E.; Richard, Stephane
PA The Salk Institute for Biological Studies, USA
SO PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001083769	A2	20011108	WO 2001-US14371	20010503
	WO 2001083769	A3	20020829		
	WO 2001083769	C2	20030206		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2000-201589P	P	20000503
	US 2000-255088P	P	20001212

AB The present invention provides the structure of the enzyme 4-diphosphocytidyl-2-C-methylerythritol (CDP-ME) synthase, a member of the cytidyltransferase family of enzymes. CDP-ME is a critical intermediate in the mevalonate-independent pathway for isoprenoid biosynthesis in a number of prokaryotic organisms, in algae, in the plastids of plants, and in the malaria parasite. Since vertebrates synthesize isoprenoid precursors using a mevalonate pathway, CDP-ME synthase and other enzymes of the mevalonate-independent pathway for isoprenoid production represent attractive targets for the structure-based design of selective **antibacterial**, herbicidal, and antimalarial drugs. Accordingly, the present invention provides methods for screening for compds. that **inhibit** enzymes of the mevalonate-independent pathway and pharmaceutical compns. and **antibacterial** formulations thereof. Further provided are methods of **inhibiting** the enzymes of the pathway and **bacterial** terpenoid synthesis and methods for treating a subject suffering from a **bacterial** infection.

L44 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:582058 HCAPLUS
DN 135:164085
TI 2-C-methyl-D-erythritol 2,4-cyclodiphosphate synthase, a novel enzyme in the nonmevalonate pathway from Escherichia coli
IN Seto, Haruo; Kuzuyama, Tomohisa
PA Japan
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001057223	A1	20010809	WO 2001-JP483	20010125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-180126P P 20000203
JP 2000-29287 A 20000207
OS CASREACT 135:164085
AB An enzyme 2-C-methyl-D-erythritol 2,4-cyclodiphosphate synthase which catalyzes a previously unknown reaction step in the non-mevalonate pathway, formation of 2-C-methyl-D-erythritol 2,4-cyclodiphosphate from 2-phospho-4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol, from Escherichia coli, its gene, and recombinant expression, are disclosed. Use of the enzyme in synthesis of isoprenoid such as ubiquinone, vitamin K2, or carotenoid, and screening of nonmevalonate pathway **inhibitors** usable as antifungal agent or herbicide, is claimed. The enzyme protein requires Mg2+ for activity and has mol. weight of about 22 kDa when measured by SDS-PAGE. Cloning of the gene, designated as ygbB, recombinant expression, and functional characterization, are described. Formation of β-carotene in E. coli transformed with ygbB gene was observed 2-Phospho-4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol was transformed to 2-C-methyl-D-erythritol 2,4-cyclodiphosphate by a novel Escherichia coli enzyme involved in the nonmevalonate pathway.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:338743 HCAPLUS
DN 134:349018
TI Cloning of isopentenyl monophosphate kinase gene from Mentha and E. coli, its expression and application
IN Croteau, Rodney B.; Lange, Bernd M.
PA Washington State University Research Foundation, USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001032907	A1	20010510	WO 2000-US30289	20001102
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6235514	B1	20010522	US 1999-434774	19991104
EP 1228238	A1	20020807	EP 2000-975555	20001102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI US 1999-434774	A1	19991104		
WO 2000-US30289	W	20001102		

AB A cDNA encoding isopentenyl monophosphate kinase (IPK) from peppermint (Mentha x piperita) has been isolated and sequenced, and the corresponding amino acid sequence has been determined Accordingly, an isolated DNA sequence (SEQ ID NO:1) is provided which codes for the expression of isopentenyl monophosphate kinase (SEQ ID NO:2), from peppermint (Mentha x piperita). In other aspects, replicable recombinant cloning vehicles are provided which code for isopentenyl monophosphate kinase, or for a base sequence sufficiently complementary to at least a portion of isopentenyl monophosphate kinase DNA or RNA to enable hybridization therewith. In yet other aspects, modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding isopentenyl monophosphate kinase. Thus, systems and methods are provided for the recombinant expression of the aforementioned recombinant isopentenyl monophosphate kinase that may be used to facilitate its production, isolation and purification in
significant amts. Recombinant isopentenyl monophosphate kinase may be used to obtain expression or enhanced expression of isopentenyl monophosphate kinase in plants in order to enhance the production of isopentenyl monophosphate kinase, or isoprenoids derived therefrom, or may be otherwise employed for the regulation or expression of isopentenyl monophosphate kinase, or the production of its products.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:672694 HCAPLUS
DN 129:272926
TI The aarC gene involved in the regulation of 2'-N-acetyltransferase activity in Providencia and its use in screening for novel **antimicrobial** agents
IN Rather, Philip N.
PA Case Western Reserve University, USA
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842875	A1	19981001	WO 1998-US6061	19980327
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5858367	A	19990112	US 1997-827190	19970327
	AU 9865890	A1	19981020	AU 1998-65890	19980327
	EP 975801	A1	20000202	EP 1998-912092	19980327
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001523097	T2	20011120	JP 1998-546016	19980327
	US 6383745	B1	20020507	US 1998-170187	19981013
PRAI	US 1997-827190	A	19970327		
	WO 1998-US6061	W	19980327		

AB The aarC gene that plays a role of the regulation of the synthesis of a key enzyme in peptidoglycan biosynthesis, the 2'-N-acetyltransferase encoded by the aac(2')-Ia gene, and that is essential for the viability of **bacteria** is cloned and characterized. The gene regulates expression of the aac(2')-Ia gene in response to cell d. Using a reporter gene under control of the aac(2')-Ia promoter can therefore be used to measure cell growth and the **bacteriostatic** and antibiotic effects of test compds. A reporter gene system using the promoter of the aac(2')-Ia gene to measure **inhibition** of aarC function is described for use in screening antibiotics. The gene may also be used as a target in the diagnosis of infection. Cloning of the aarC gene by complementation is described.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:663612 HCAPLUS
DN 130:33770
TI Functional analysis of the Helicobacter pylori principal sigma subunit of RNA polymerase reveals that the spacer region is important for efficient transcription
AU Beier, Dagmar; Spohn, Gunther; Rappuoli, Rino; Scarlato, Vincenzo
CS Department of Molecular Biology, Chiron SpA, IRIS Research Institute, Siena, 53100, Italy
SO Molecular Microbiology (1998), 30(1), 121-134
CODEN: MOMIEE; ISSN: 0950-382X
PB Blackwell Science Ltd.
DT Journal
LA English
AB We have cloned the rpoD gene encoding the principal sigma (σ) factor of Helicobacter pylori. The deduced amino acid sequence reveals a predicted polypeptide of 676 residues that has amino acid homol. with the principal σ factors of a number of divergent prokaryotes. We have

designated this factor σ80. Amino acid sequence anal. suggests that region 1.1 is missing in σ80 and that a region with homol. to a regulatory protein from Bacillus subtilis phage SPO1 is present. Genetic studies have indicated that σ80 is not compatible with the transcriptional machinery of Escherichia coli. However, in vitro σ80 could be assembled into the E. coli RNA polymerase and could bind to E. coli and H. pylori promoters, suggesting that the σ80-containing RNA polymerase has the same stoichiometry as the native complex. By exchanging protein domains between E. coli and H. pylori σ factors, we demonstrate that the σ80 domain **inhibiting** transcription from E. coli promoters is confined within the non-conserved spacer region, implying that the spacer region of prokaryotic primary σ factors plays an important role in the process of transcription. Consistent with its restricted niche and with the availability of a very restricted number of transcriptional regulators, H. pylori may have evolved a spacer region of the σ factor to modulate total transcription and to quickly respond to microenvironmental changes.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 22 OF 34 MEDLINE on STN DUPLICATE 2
AN 2003125371 MEDLINE
DN PubMed ID: 12639570
TI Functional expression and characterization of EryA, the erythritol kinase of Brucella abortus, and enzymatic synthesis of L-erythritol-4-phosphate.
AU Lillo Antonietta M; Tetzlaff Charles N; Sangari Felix J; Cane David E
CS Department of Chemistry, Brown University, Providence, RI 02912-9108, USA.
NC GM30301 (NIGMS)
SO Bioorganic & medicinal chemistry letters, (2003 Feb 24) 13 (4) 737-9. Journal code: 9107377. ISSN: 0960-894X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200311
ED Entered STN: 20030318
Last Updated on STN: 20031217
Entered Medline: 20031120
AB The eryA **gene** of the **bacterial** pathogen Brucella abortus has been functionally expressed in Escherichia coli. The resultant EryA was shown to catalyze the ATP-dependent conversion of erythritol to L-erythritol-4-phosphate (L-E4P). The steady state kinetic parameters of this reaction were determined and the enzyme was used to prepare L-E4P which was shown to be a weak **inhibitor** of 2-C-methyl-D-erythritol-4-phosphate cytidyltransferase (**YgbP**).

L44 ANSWER 23 OF 34 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2002328005 EMBASE
TI Peritoneal fibrosis and its prevention.
AU Hung K.-Y.; Tsai T.-J.; Chen W.-Y.
CS Dr. T.-J. Tsai, Department of Internal Medicine, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei, Taiwan,Province of China. paul@ha.mc.ntu.edu.tw
SO Nephrology, (2002) 7/5 (227-232).
Refs: 60
ISSN: 1320-5358 CODEN: NEPHF2
CY Australia
DT Journal; General Review

FS 005 General Pathology and Pathological Anatomy
028 Urology and Nephrology
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Peritoneal fibrosing syndrome (**PFS**) is composed of a wide spectrum of peritoneal alterations observed in patients under peritoneal dialysis (PD). Long-term peritoneal exposure to unphysiological PD solutions and recurrent **bacterial** peritonitis had been claimed as the most common causes predisposing to the development of **PFS** in a PD population. With the advances in molecular research, physicians and pathologists recognized that peritoneal injury and the accompanied accumulation of extracellular matrix (ECM) within the peritoneum are key events leading to **PFS**. Bioincompatible solution and it's related products, inflammatory mediators, growth factors as well as cytokines in the peritoneal cavity are contributing factors. Therapeutic strategies **antagonizing** these mediators and/or their downstream intracellular signalling pathways with either drug molecules or **gene** transfer may have potential for the prevention or treatment of **PFS**.

L44 ANSWER 24 OF 34 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:338387 BIOSIS
DN PREV200300338387
TI SAH/MTA nucleosidase: A novel target for broad spectrum antibiotic development.
AU Chen, S. [Reprint Author]; Margosiak, S. A. [Reprint Author]; Feher, V. [Reprint Author]; Pinko, C. [Reprint Author]; Zaidi, S. [Reprint Author]; Appelt, K. [Reprint Author]
CS Quorex Pharmaceuticals Inc, Carlsbad, CA, USA
SO Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2002) Vol. 42, pp. 197. print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA, USA. September 27-30, 2002. American Society for Microbiology.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB Background: S-adenosyl homocysteine/methylthioadenosine (SAH/MTA) nucleosidase is a product of the highly conserved **pfs gene**. The **pfs gene** is essential in all tested gram-positive pathogenic **bacteria** and does not appear to have a functional or structural mammalian homologue. Functionally, **inhibition** of SAH/MTA nucleosidase activity eliminates the downstream synthesis of the quorum sensing autoinducer AI-2. In addition, the accumulation of the toxic SAH and MTA substrates elicits **inhibition** of various essential methyltransferase reactions and affects the recycling of adenine and methionine that are necessary for DNA and protein synthesis, respectively. Methods: We examined the enzymatic activity and active-site structural information of SAH/MTA nucleosidases from various pathogens in order to assess its validity as an effective broad-spectrum antimicrobial target. The enzyme from E. coli and several clinically important pathogenic **bacteria** including Staphylococcus aureus, Streptococcus pneumoniae, Enterococcus faecalis and Haemophilus influenzae were cloned, expressed purified, and catalytically characterized. The search for nucleosidase **inhibitors** utilized

structure-based compound design and synthesis of focused combinatorial chemical libraries. Results: The Km and Vmax values for MTA are quite similar to E. coli across all studied pathogenic nucleosidases. We have identified a number of structurally unique small molecule **inhibitors**. Crystallization and X-ray structural determination of E. coli and pathogenic MTA/SAH nucleosidases both in the apo-form and complexed with potent **inhibitors** revealed a highly conserved active site amenable to structure-based drug design. Conclusion: The conservation of the MTA/SAH nucleosidase active site with respect to the primary sequence, catalytic efficiency, and 3D structure is high. MTA/SAH nucleosidase appears to be a valid target for new and unique broad-spectrum antibiotics.

L44 ANSWER 25 OF 34 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:338385 BIOSIS
DN PREV200300338385
TI Characterization of 5'-Methylthioadenosine Nucleosidase/S-Adenosylhomocysteine Nucleosidase (**Pfs**) mutant phenotypes in pathogenic and non-pathogenic **bacteria**.
AU Brett, P. J. [Reprint Author]; Vasu, S. K. [Reprint Author]; Grant, C. C. R. [Reprint Author]; Levin, J. C. [Reprint Author]; McKenzie, D. T. [Reprint Author]
CS Quorex Pharmaceuticals, Carlsbad, CA, USA
SO Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2002) Vol. 42, pp. 197. print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA, USA. September 27-30, 2002. American Society for Microbiology.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB Background: 5'-Methylthioadenosine Nucleosidase/S-Adenosylhomocysteine Nucleosidase (**Pfs**) catalyzes the hydrolysis of 5'-methylthioadenosine (MTA) to 5'-methylthioribose (MTR) and S-adenosylhomocysteine (SAH) to S-ribosylhomocysteine (SRH) in prokaryotes but not mammalian cells. Since MTA and SAH are potent **inhibitors** of important cellular processes in prokaryotes, **Pfs** represents an attractive target for the development of novel broad-spectrum antimicrobial compounds. In the present study we have examined the importance of **Pfs** activity in a variety of pathogenic and non-pathogenic **bacterial** species. Methods: Allelic exchange and insertional inactivation mutagenesis strategies were used to construct **pfs** null mutations in E. coli, S. typhimurium, Haemophilus influenzae, Enterococcus faecalis, Streptococcus pneumoniae and Streptococcus pyogenes. Growth curves were conducted in both rich and chemically defined media. AI-2 production was quantitated using the Vibrio harveyi reporter assay. Carbohydrate utilization profiles were determined using API 50 CH strips incubated under anaerobic and aerobic conditions. An A/J mouse model of acute sepsis was used to assess the virulence phenotype of the S. typhimurium **pfs** mutant. Results: Phenotypic analysis of the E. coli and S. typhimurium **pfs** mutants demonstrated attenuated growth profiles, the inability to synthesize AI-2 and altered carbohydrate utilization profiles in comparison to the parental strains. The S. typhimurium **pfs** null mutant also demonstrated proliferation deficiencies in Hela cells and a >30 fold decrease in virulence relative to the parental strain. We were unable to isolate H. influenzae, E. faecalis, S. pyogenes and S.

pneumoniae **pfs** null mutants. Conclusion: Although **Pfs** activity is non-essential in E. coli and S. typhimurium, mounting evidence suggests that it may be essential in H. influenzae, E. faecalis, S. pyogenes, S. pneumoniae.

L44 ANSWER 26 OF 34 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:176638 BIOSIS
DN PREV200200176638
TI Targeted mutagenesis of the **gene** encoding the flagellar hook protein in the Lyme disease spirochete Borrelia burgdorferi.
AU Sal, M. [Reprint author]; Motaleb, M. A. [Reprint author]; Charon, N. W. [Reprint author]
CS West Virginia University, Morgantown, WV, USA
SO Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 122. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society for Microbiology.
ISSN: 1060-2011.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 6 Mar 2002
Last Updated on STN: 6 Mar 2002
AB Borrelia burgdorferi is a wave-like, motile, pathogenic spirochete that causes Lyme disease. Between 7-11 periplasmic flagella (**PFs**) are attached at the ends of the cell and extend inward along the cell cylinder beneath the outer membrane sheath. These **PFs**, composed of basal body, hook, and filament, are similar in structure to flagella from other **bacteria**. Recent results from our laboratory have shown mutant cells defective in the PF filament protein, FlaB, are no longer wave-like but are rod shaped. These mutants were also found to be non-motile, indicating that the **PFs** are involved in both morphology and motility. Furthermore, these mutants failed to produce the putative flagella filament sheath protein, FlaA, suggesting that FlaB may be involved in regulating flagella synthesis. Previous evidence indicated that the regulation of B. burgdorferi PF synthesis differs from that in other **bacteria**, as the transcription factor sigma28 is not involved in its PF regulation. To further test the notion that **PFs** are involved in both morphology and motility, we inactivated the **gene** encoding the flagellar hook protein, flgE, by targeted mutagenesis using a kanamycin resistance cassette (kan). PCR analysis of the recombinants obtained indicated an insertion of the 1.3 kb kan cassette within the flgE **gene**. The mutant cells displayed an altered rod-shaped morphology and a loss of motility. These results further extend those obtained with flaB mutants that indicated **PFs** were involved in both motility and morphology. Furthermore, Western blot analysis confirmed that the flgE mutant cells fail to produce flagella filament proteins FlaA and FlaB. Remarkably, all three of the flagellar **genes**, flgE, flaA, and flaB, map in different operons in B. burgdorferi. These latter results indicate that **inhibition** of flagellar hook protein synthesis negatively impacts the synthesis of both FlaA and FlaB. Taken together, the results obtained not only support the importance of the **PFs** in both the motility and morphology of B. burgdorferi, but also suggest that the flagellar hook protein plays a role necessary for both FlaA and FlaB synthesis.

L44 ANSWER 27 OF 34 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-239393 [23] WPIX

DNC C2003-061491
TI New acyclic or cyclic organophosphorus compounds, are gamma-delta-T cell activators useful e.g. as medicaments for treating asthma, chronic bronchitis, ulcerative colitis, autoimmune diseases or allergies.
DC B05 C01
IN ALTINCICEK, B; EBERL, M; HINTZ, M; JOMAA, H; KOLLAS, A; REICHENBERG, A; WIESNER, J; WOLF, O
PA (JOMA-N) JOMAA PHARMAKA GMBH; (BIOA-N) BIOAGENCY AG
CYC 101
PI WO 2003009855 A2 20030206 (200323)* GE 33
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
DE 10135395 A1 20030213 (200323)
DE 10134705 A1 20030206 (200326)
EP 1408984 A2 20040421 (200427) GE
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
ADT WO 2003009855 A2 WO 2002-EP7986 20020718; DE 10135395 A1 DE 2001-10135395 20010725; DE 10134705 A1 DE 2001-10134705 20010720; EP 1408984 A2 EP 2002-776913 20020718, WO 2002-EP7986 20020718
FDT EP 1408984 A2 Based on WO 2003009855
PRAI DE 2001-10135395 20010725; DE 2001-10134705 20010720
AB WO2003009855 A UPAB: 20030407
NOVELTY - Organophosphorus compounds (I), including acyclic and cyclic phosphates, pyrophosphates, triphosphates, phosphonates and phosphinates, are new.

DETAILED DESCRIPTION - Organophosphorus compounds of formula (I) are new.

R1 = Me, CHO, optionally substituted hydroxymethyl or CH2R31;

R31 = OH, optionally substituted phosphate or optionally substituted pyrophosphate;

R33 = H, optionally substituted phosphate or optionally substituted pyrophosphate;

R3 = H, optionally substituted 1-26C alkyl, optionally substituted 1-26C hydroxyalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted 2-26C alkenyl, optionally substituted 2-26C alkynyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted phosphate, silyl, nucleoside, nucleoside mon-, di- or triphosphate, deoxynucleotide, cation of an (in)organic base (especially a Group I-III non-transition metal, optionally substituted ammonium, ethylene diamine-derived or aminoacid-derived cation) or OR34;

R34 = as R3;

X1 = O or -C(Y1)(Y2)-;

X2 = OR6, -X3-P(O)(OR7)(OR8), -Z1-P(O)(OR4)-X3 or a group as defined for X1 or forming a ring with C1;

X3 = -Z2-P(O)(OR5)-X4 or a group as defined for X1 or forming a ring with C1;

R4, R5 = as R3;

R7, R8 = as R34;

Z1, Z2 and X4 (forming a ring with C1) = as X1;

R2 = H, OH, alkoxy, phenoxy, benzyloxy, optionally substituted phosphate or optionally substituted pyrophosphate;

X2 = O or -C(Y1)(Y2)-; and

Y1, Y2 = H, OH, halo, NH2, 1-9C alkoxy or 1-9C alkylthio; or together form =O.

Provided that:

(1) a double bond is optionally presence between C1 and C2 or C2 and C3; and

(2) R31 and R3 are not simultaneously present in the molecule.

AN INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Antiasthmatic; antiinflammatory; antiulcer; neuroprotective; osteopathic; immunosuppressive; antiallergic; virucide; hepatotropic; cytostatic; **antibacterial**; antirheumatic; antiarthritic; thyromimetic; dermatological; antidiabetic; antianemic; cardiant; ophthalmological; antiparasitic; herbicide.

MECHANISM OF ACTION - alpha / delta -T Cell activator.

Trisodium 4-hydroxy-3-methyl-2-butenyl pyrophosphate (Ia) had 10000-fold stronger activity than isopentenyl diphosphate in activating alpha / delta -T cells in vitro.

USE - The use of (I) is claimed for activating alpha / delta -T cells; as substrates or products in processes for carrying out enzyme **inhibition** tests and screening enzyme **inhibitors** (specifically where the enzyme is a LytB or **GcpE** enzyme); for determining the activation of LytB or **GcpE** enzymes; and in medicaments for the treatment or prophylaxis of diseases in human or veterinary medicine, specifically where the diseases are respiratory tract diseases (especially asthma or chronic bronchitis), Crohn's disesae, ulcerative colitis, multiple sclerosis, bone diseases (especially osteoporosis), immune or autoimmune diseases, allergies, hepatitis C infections, tumors induced by microorganisms (especially papilloma viruses) or gastrointestinal ulcers induced by Helicobacter. Further specific disorders to be treated include rheumatoid arthritis, Hashimoto thyroiditis, myasthenia gravis, lupus erythematodes, diabetes mellitus, primary biliary cirrhosis, active chronic hepatitis, Addison's disease, polymyositis, dermatomyositis, autoimmune hemolytic anemia, cardiac muscle and pericardial inflammation, scleroderma, uveitis, pemphigus vulgaris, pemphigoid, pernicious anemia, autoimmune atrophic gastritis and parasitic infections. (I) also show herbicidal activity.

ADVANTAGE - (I) have potent alpha / delta -T cell activating and immune system regulating action.

Dwg.0/0

L44 ANSWER 28 OF 34 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-113392 [11] WPIX
DNC C2003-029228
TI Enriching intermediates in the mevalonate-independent pathway of isoprenoid synthesis, useful for therapeutic activation of T cells, comprises altering enzymatic activity in the pathway.
DC B04 D16
IN ALTINCICEK, B; EBERL, M; JOMAA, H
PA (JOMA-N) JOMAA PHARMAKA GMBH; (BIOA-N) BIOAGENCY AG
CYC 101
PI DE 10119905 A1 20021024 (200311)* 10
WO 2002095011 A2 20021128 (200311) GE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
EP 1381686 A2 20040121 (200410) GE

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

ADT DE 10119905 A1 DE 2001-10119905 20010423; WO 2002095011 A2 WO 2002-EP4134 20020413; EP 1381686 A2 EP 2002-737952 20020413, WO 2002-EP4134 20020413

FDT EP 1381686 A2 Based on WO 2002095011

PRAI DE 2001-10119905 20010423

AB DE 10119905 A UPAB: 20040505

NOVELTY - Enriching intermediates (A) in the mevalonate-independent isoprenoid synthesis pathway (MEP-way) comprises deleting, inactivating or otherwise altering a **gene** (I) in the pathway, in a cell or organism, so that the enzymatic activity of the product of (I) is reduced or made non-natural.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) Similar method that comprises treating the cell or organism with enzyme **inhibitors**; and

(2) (A) produced by the new methods.

ACTIVITY - Antiasthmatic; Antiinflammatory; Antiulcer; Neuroprotective; Immunosuppressive; Antiallergic; Osteopathic.

MECHANISM OF ACTION - T cell activation, resulting in increased immune responses or development of immune tolerance. V gamma + T cells isolated from blood of healthy humans were incubated for 72 hours in medium containing an (A)-enriched fraction produced by a LytB-deletion mutant of Escherichia coli. Expression of the CD25 activation marker was then measured by flow cytometry. At a dilution of 500, this fraction activated about 90% of the cells compared to about 55% for a similar fraction from wild-type **bacteria** and 20% for a **GcpE** -deletion mutant and about 50% for 10 micro M isopentenyl pyrophosphate (reference).

USE - The method is used for production of (A), especially substrates of the **GcpE** and LytB enzymes that activate gamma / delta T cells. (A) and their derivatives are useful for:

(i) determining activity of **GcpE** and LytB, e.g. to identify their **inhibitors**;

(ii) to activate gamma / delta T cells; and

(iii) as pharmaceuticals

Dead or live cells or organisms enriched in (A) can be used similarly for treatment, in humans or animals, of asthma, Crohn's diseases, ulcerative colitis, multiple sclerosis, chronic bronchitis, (auto)immune diseases, allergies; bone diseases and osteoporosis (all claimed), also a wide variety of other diseases and for improving the immune response against tumors.

Dwg.0/2

L44 ANSWER 29 OF 34 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2002-075235 [10] WPIX

CR 2002-062235 [08]

DNC C2002-022425

TI Use of autoinducer-2 agonists or **antagonists** for regulating activity of autoinducer-2 receptor, regulating **bacterial** growth and pathogenesis, also antibiotic compositions.

DC B02 B03 B04 C06 D16

IN BASSLER, B L; DAMMEL, C S; SCHAUDER, S; SHOKAT, K; STEIN, J; SURETTE, M G; DAMMEL, C

PA (QUOR-N) QUOREX PHARM INC; (UYPR-N) UNIV PRINCETON; (UYTE-N) UNIV TECHNOLOGIES INT INC; (BASS-I) BASSLER B L; (DAMM-I) DAMMEL C; (SCHA-I) SCHAUDER S; (SHOK-I) SHOKAT K; (STEI-I) STEIN J; (SURE-I) SURETTE M G

CYC 95

PI WO 2001085664 A2 20011115 (200210)* EN 134

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001059734 A 20011120 (200219)
EP 1282415 A2 20030212 (200312) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
US 6559176 B1 20030506 (200338)
JP 2003532698 W 20031105 (200377) 186
US 2004097402 A1 20040520 (200434)
ADT WO 2001085664 A2 WO 2001-US15221 20010510; AU 2001059734 A AU 2001-59734 20010510; EP 1282415 A2 EP 2001-933298 20010510, WO 2001-US15221 20010510; US 6559176 B1 Provisional US 2000-203000P 20000510, Provisional US 2000-254398P 20001207, US 2001-853832 20010510; JP 2003532698 W JP 2001-582266 20010510, WO 2001-US15221 20010510; US 2004097402 A1 Provisional US 2000-202999P 20000510, Provisional US 2000-203000P 20000510, Provisional US 2000-254398P 20001207, Div ex US 2001-853832 20010510, US 2002-300818 20021119
FDT AU 2001059734 A Based on WO 2001085664; EP 1282415 A2 Based on WO 2001085664; JP 2003532698 W Based on WO 2001085664; US 2004097402 A1 Div ex US 6559176
PRAI US 2000-254398P 20001207; US 2000-203000P 20000510;
US 2001-853832 20010510; US 2000-202999P 20000510;
US 2002-300818 20021119
AB WO 200185664 A UPAB: 20040527
NOVELTY - The use of autoinducer-2 (AI-2) agonists or **antagonists** for regulating activity of autoinducer-2 receptor, regulating **bacterial** growth and pathogenesis is new. Also new are synergistic antibiotic compositions comprising **inhibitors** of the quorum-sensing pathway of a microorganism.

DETAILED DESCRIPTION - A method for regulating the activity of autoinducer-2 receptor comprises contacting the receptor with AI-2 agonist or **antagonist** compound. INDEPENDENT CLAIMS are included for the following:

(1) a method for identifying a compound that regulates the activity of AI-2 by contacting AI-2 with the compound and comparing activity in the presence and absence of the compound;

(2) a method for identifying an AI-2 analog that regulates activity of AI-2 by contacting a **bacterial** cell comprising biosynthetic pathways which will produce a detectable amount of light in response to AI-2 with the AI analog, and comparing the amount of light produced by the cell in the presence of the AI-2 with the amount produced in the presence of AI-2 and AI-2 analog;

(3) a method for detecting an autoinducer associated **bacterial** biomarker by contacting a **bacterial** cell with an autoinducer molecule to promote induction of a **bacterial** biomarker; and detecting the biomarker;

(4) a method for identifying a compound that affects AI-2 binding to an AI-2 receptor, by contacting AI-2 and AI-2 receptor with the compound; contacting with a cell comprising biosynthetic pathways that produce light in response to AI-2 binding; and measuring light production;

(5) a method for producing AI-2 by contacting S adenosylhomocysteine with a LuxS protein; and/or contacting S ribosylhomocysteine with a LuxS polypeptide;

(6) AI-2 prepared as described in (5);

(7) a synergistic antibiotic composition comprising an antibiotic and

an **inhibitor** of the quorum-sensing pathway of a microorganism, and its use for treating infections, and medical devices comprising the composition; and

(8) a medical device comprising at least 1 antimicrobial compound of formula (I).

X = O, S or N;

R1a = H, OH, alkyl, acyl, amido, OH, NH2, thio or aryl;

R1b = R1a or mercapto; or

R1a+R1b = double bond;

R2 = H, alkyl or halo;

R3 = H, alkyl, acyl, amido, OH, NH2, thio or aryl;

R4 = H, if X is N, or is absent if X is O or S; or

C4 and C5 = optionally be joined by a double bond.

ACTIVITY - Antibiotic; **Antibacterial**; Dermatological; Vulnerary.

Tests were carried out to determine activity of 2-ethyl-4-hydroxy 5-methyl-3(2H)-furanone (Ia), alone and in combination with e.g. vancomycin (VM) or ciprofloxacin (CF), against Streptococcus pyogenes (ATCC 19615) or Staphylococcus aureus (ATCC 25923). MIC values were: (a) VM alone, 100 g/ml; (b) VM + (Ia) (12.5 g/ml) 1.6 micro g/ml; (c) (Ia) alone, greater than 100 g/ml; (d) CF alone, 0.8 g/ml; (e) CF + (Ia) (25 g/ml), 0.4 g/ml.

MECHANISM OF ACTION - Autoinducer-2 (AI-2) modulators.

USE - For treating pathogen-associated disease states. The compounds and antibiotic compositions can be used to **inhibit bacterial** cell growth and/or biofilm formation on a medical device, particularly for promoting growth of skin graft replacements used in the treatment of burns and ulcers. They may also be used to aid wound repair, and to **inhibit bacterial** cell growth and biofilm formation in or on products or devices used for personal hygiene. Dwg.0/34

L44 ANSWER 30 OF 34 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-235213 [24] WPIX
DNC C2001-070559
TI New Staphylococcus aureus **kdtB** polynucleotides and polypeptides, useful for screening antimicrobial compounds and for treating or diagnosing microbial diseases, e.g. lung or cerebral abscess, toxic shock syndrome or wound infections.
DC B04 D16
IN THROUP, J P; VAN HORN, S
PA (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
CYC 19
PI WO 2001018249 A1 20010315 (200124)* EN 37
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP
ADT WO 2001018249 A1 WO 2000-US24478 20000907
PRAI US 1999-393615 19990910
AB WO 200118249 A UPAB: 20010502
NOVELTY - An isolated **kdtB** polynucleotide (I) from Staphylococcus aureus comprising a fully defined sequence (S1) of 483 base pairs (bp) encoding a polypeptide (II) with a fully defined sequence (S2) of 160 amino acids (aa) as given in the specification, is new.

DETAILED DESCRIPTION - An isolated **kdtB** polynucleotide (PN) (I) comprising:

(a) an isolated PN encoding a polypeptide (PP) that is at least 95% identical to S2 over its entire length;

(b) an isolated PN at least 95% identical to a PN encoding S2;

(c) an isolated PN at least 95% identical to S1 over its entire

length;

(d) an isolated PN comprising a nucleotide (NT) sequence encoding (II);

(e) the PN of S1;

(f) an isolated PN of at least 30 NT in length obtainable by screening an appropriate library under stringent hybridization conditions with a probe with the sequence S1 or its fragment of at least 30 NT in length;

(g) an isolated PN encoding a mature PP expressed by the **kdtB gene** contained in Staphylococcus aureus; or

(h) a PN sequence complementary to any one of (a)-(g).

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated **kdtB** PP (II) comprising:

(a) an isolated PP containing an aa sequence at least 95% identical to S2 over its entire length;

(b) an isolated PP comprising or is S2; or

(c) a PP that is encoded by a recombinant PN containing S1;

(2) treating an individual:

(a) in need of enhanced activity or expression of or immunological response to (II) comprising administering to the individual an **antagonist** of (II);

(b) having need to **inhibit** activity of (II) comprising administering:

(i) an **antagonist** of (II);

(ii) a nucleic acid molecule that **inhibits** the expression of (I);

(iii) a polypeptide that competes with (II) for its ligand, substrate or receptor; or

(iv) a polypeptide that induces an immunological response to (II) in the individual;

(3) diagnosing or prognosing a (susceptibility to a) disease in an individual related to expression or activity of (II) comprising:

(a) determining the presence or absence of a mutation in (I) in an organism in the individual; or

(b) analyzing for the presence or amount of (II) expression in a sample derived from the individual;

(4) producing a host cell comprising an expression system or its membrane that expresses (II) comprising transforming or transfecting the cell with an expression system comprising (I);

(5) a host cell (III) or a membrane expressing (II);

(6) producing (II) comprising culturing (III);

(7) an antibody immunospecific for (II);

(8) screening/identifying compounds that agonize or inhibit the function of (II) comprising:

(a) measuring the binding of a candidate compound to (II), (III) or its membranes or its fusion protein by means of a label (in)directly associated with the candidate compound, or in the presence of a labeled competitor;

(b) testing whether the candidate compound results in a signal generated by activation or inhibition of (II), using detection systems appropriate to (III) or its membranes bearing (II);

(c) mixing a candidate compound with a solution comprising (II) measuring the activity of the kdtB polypeptide in the mixture, and comparing the activity of the mixture to a standard; or

(d) detecting the effect of a candidate compound on the production of mRNA encoding (II) in cells, using for instance, an enzyme linked immunosorbant assay; and

(9) an (ant)agonist of (II).

ACTIVITY - Antibiotic; antithyroid; ophthalmological; vulnerary;

antiarthritic; antibacterial. No biological data is given.

MECHANISM OF ACTION - KdtB antagonist; kdtB agonist.

USE - The kdtB polypeptide and polynucleotide are useful for treating microbial diseases, especially diseases caused by Staphylococcus aureus, e.g. otitis media, bacterial tracheitis, thyroiditis, lung abscess, infective endocarditis, splenic abscess, cerebral abscess, conjunctivitis, toxic shock syndrome, impetigo, wound infection or septic arthritis. These are also useful as diagnostic reagents for diagnosing or staging of a disease, or for evaluating the response of an infectious organism to drugs. The kdtB polypeptide and polynucleotide are useful for screening (ant)agonists of the kdtB polypeptide, as well as for screening compounds for antimicrobial activity.

Dwg.0/0

L44 ANSWER 31 OF 34 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-182934 [18] WPIX
DNC C2001-054615
TI New **kdtB** polypeptides and polynucleotides of Streptococcus pneumoniae for diagnosing or prognosing a disease or susceptibility to disease in an individual related to expression or activity of the polypeptide.
DC B04 D16
IN CHALKER, A F; HOLMES, D J; INGRAHAM, K A; SO, C Y; THROUP, J P; VAN HORN, S; WARREN, R L
PA (CHAL-I) CHALKER A F; (HOLM-I) HOLMES D J; (INGR-I) INGRAHAM K A; (SOCY-I) SO C Y; (THRO-I) THROUP J P; (VHOR-I) VAN HORN S; (WARR-I) WARREN R L; (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
CYC 20
PI WO 2001009167 A1 20010208 (200118)* EN 39
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP
US 6277597 B1 20010821 (200150)
US 2002115191 A1 20020822 (200258)
ADT WO 2001009167 A1 WO 2000-US20743 20000731; US 6277597 B1 US 1999-366623 19990803; US 2002115191 A1 Div ex US 1999-366623 19990803, US 2001-927070 20010809
PRAI US 1999-366623 19990803; US 2001-927070 20010809
AB WO 200109167 A UPAB: 20010402
NOVELTY - An isolated polypeptide (I):

(1) comprising 95% identity over the entire length of a **kdtB** polypeptide sequence of 162 amino acids (S2), given in the specification;

(2) comprising a sequence of (S2);

(3) that is (S2); or

(4) that is encoded by a recombinant **kdtB** polynucleotide having a sequence of 489 nucleotides (S1), given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) which:

(i) comprises a polynucleotide sequence encoding a polypeptide which has 95% identity over the entire length of (S2);

(ii) comprises a polynucleotide sequence that has 95% identity over the entire length of a polynucleotide sequence encoding (S2);

(iii) comprises a nucleotide sequence which has 95% identity over the entire length of (S1);

(iv) comprises a nucleotide sequence encoding (S2);

(v) is a polynucleotide comprising a sequence of (S1);

(vi) is a polynucleotide of 30 nucleotides in length obtainable by screening an appropriate library under stringent hybridization conditions

with a probe having a sequence of (S1) or its fragment having 30 nucleotides;

(vii) encodes a mature polypeptide expressed by the **kdtB gene** from Streptococcus pneumoniae; or

(viii) is a polynucleotide sequence complementary to the all the above mentioned polynucleotide sequences;

(2) treating an individual:

(i) in need of enhanced activity or expression of an immunological response to (I) comprising administering an **antagonist** to (I);

(ii) having need to **inhibit** activity or expression of (I) comprising administering:

(a) an **antagonist** to (I);

(b) a nucleic acid that **inhibits** the expression of a polynucleotide encoding (I);

(c) a polypeptide that competes with (I) for its ligand, substrate or receptor; or

(d) a polypeptide that induces an immunological response to (I) in the individual;

(3) diagnosing or prognosing a disease or a susceptibility to a disease in an individual related to expression or activity of (I) comprising determining the presence or absence of a mutation in the nucleotide sequence encoding (I) in an organism in the individual or analyzing for the presence or level of expression of (I) in a sample derived from the individual;

(4) producing (I) comprising culturing a host cell to produce (I);

(5) producing a host cell comprising an expression system or its membrane expressing (I) involving transforming or transfecting the cell with an expression system comprising a polynucleotide capable of producing (I) when the expression system is present in a compatible host cell which under appropriate culture conditions produces (I);

(6) a host cell (III) or membrane expressing (I);

(7) an antibody (IV) immunospecific for (I);

(8) screening to identify compounds that agonize or that **inhibit** the function of (I) involving:

(a) measuring the binding of the candidate compound to (I) (or to the cells or membranes bearing the polypeptide) or a fusion protein by means of a label directly or indirectly associated with the candidate compound;

(b) measuring the binding of the candidate compound to the polypeptide or its fusion protein in the presence of a labeled competitor;

(c) testing whether the candidate compounds results in a signal generated by activation or inhibition of the polypeptide using appropriate detection systems;

(d) mixing a candidate compound with a solution comprising (I) to form a mixture, measuring the activity of the polypeptide in the mixture and comparing the activity of the mixture to a standard; or

(e) detecting the effect of the candidate compound on the production of mRNA encoding the polypeptide and the polypeptide in cells, using an enzyme linked immunosorbant assay (ELISA); and

(9) an agonist (V) or antagonist (VI) of (I).

ACTIVITY - Cytostatic; antiinflammatory; antiulcer; antimicrobial. No biological data is given.

MECHANISM OF ACTION - kdtB antagonist; gene therapy.

USE - An agonist (V) of (I) can treat an individual in need of enhanced activity or expression of or immunological response to (I), and an antagonist (VI) can treat an individual in need of inhibiting activity or expression of (I). A nucleic acid that inhibits expression of a polynucleotide sequence encoding (I), a polypeptide that competes with (I) for its ligand, substrate or receptor, or a polypeptide that induces an immunological response to the polypeptide in the individual, is

administered for inhibiting the activity or expression of (I). (I) and a polynucleotide (II) encoding (I) are used as diagnostic reagents, and can diagnose or prognose a disease or susceptibility to a disease in an individual related to expression or activity of (I) (claimed). (V) can treat microbial infections and conditions associated with such infections. Fragments of (II) are used as probes or primers and to synthesize full length kdtB polynucleotides. (I) and (II) are used as research reagents and materials for discovery of treatments of and diagnostics for diseases. Detection of kdtB polynucleotides and/or polypeptides provides a method for diagnosing a disease, staging a disease, or detecting a response of an infectious organism to drugs. (I), (II), and (IV) are used to configure screening methods for detecting the effect of compounds on the production of mRNA and/or polypeptides in cells, and also to identify agonists or antagonists of (I). (I) is also used to identify membrane bound or soluble receptors. (I) and (II) are used in structure based design of an agonist or antagonist and for treating abnormal conditions related to either excess or under expression, or an elevated activity or a decreased activity of kdtB polypeptide and/or polynucleotides. (II) can be used in the discovery and developments of antibacterial compounds and the (I) can be used as a target for screening antibacterial drugs. The polynucleotide sequences encoding the amino terminal regions of (I) or Shine-Dalgarno or other translation facilitating sequences of the respective mRNA can be used to construct antisense sequences to control the expression of the coding sequence of interest. (I), (II), (V), and (VI) are used to interfere with the initial physical interaction between a pathogen and a mammalian host responsible for sequelae of infection. The molecules are used:

(i) in preventing adhesion of gram positive and/or gram negative bacteria to eukaryotic extracellular matrix proteins, in-dwelling devices, or to extracellular matrix proteins in wounds;

(ii) to block bacterial adhesion between eukaryotic extracellular matrix proteins and bacterial kdtB proteins that mediate tissue damage; and/or

(iii) to block the normal progression of pathogenesis in infections initiated other than by the implantation of in-dwelling devices or by other surgical techniques.

(V) or (VI) is used for treating Helicobacter pylori infection which causes cancers such as gastrointestinal carcinoma and also to prevent, inhibit and/or cure gastric ulcers and gastritis.

Dwg.0/0

L44 ANSWER 32 OF 34 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-025196 [03] WPIX
CR 1999-602446 [52]; 1999-611286 [52]; 1999-633798 [54]; 2000-147167 [13]; 2000-171242 [15]; 2000-182322 [16]; 2000-283424 [24]; 2000-283543 [24]; 2000-303195 [26]
DNN N2001-019602 DNC C2001-007801
TI Incorporating **gcpE** and yfgB **genes** into viruses and cells, for increasing isoprenoid content and identifying e.g. antimicrobial agents, comprises using DNA sequences from **bacteria** or parasites.
DC B04 C06 C07 D16 S03
IN JOMAA, H
PA (JOMA-I) JOMAA H; (JOMA-N) JOMAA PHARMAKA GMBH; (JOMA-N) JOMAA PHARM GMBH
CYC 92
PI WO 2000072022 A1 20001130 (200103)* GE 36
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES

FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

DE 19923568 A1 20001123 (200103)
AU 2000050694 A 20001212 (200115)
EP 1179187 A1 20020213 (200219) GE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
BR 2000011289 A 20020226 (200223)
NO 2001005657 A 20020117 (200224)
CN 1351715 A 20020529 (200258)
HU 2002001386 A2 20020828 (200264)
JP 2003500073 W 20030107 (200314) 40
MX 2001011894 A1 20030701 (200366)

ADT WO 2000072022 A1 WO 2000-EP4592 20000520; DE 19923568 A1 DE 1999-1023568 19990521; AU 2000050694 A AU 2000-50694 20000520; EP 1179187 A1 EP 2000-935082 20000520, WO 2000-EP4592 20000520; BR 2000011289 A BR 2000-11289 20000520, WO 2000-EP4592 20000520; NO 2001005657 A WO 2000-EP4592 20000520, NO 2001-5657 20011120; CN 1351715 A CN 2000-807856 20000520; HU 2002001386 A2 WO 2000-EP4592 20000520, HU 2002-1386 20000520; JP 2003500073 W JP 2000-620359 20000520, WO 2000-EP4592 20000520; MX 2001011894 A1 WO 2000-EP4592 20000520, MX 2001-11894 20011121

FDT AU 2000050694 A Based on WO 2000072022; EP 1179187 A1 Based on WO 2000072022; BR 2000011289 A Based on WO 2000072022; HU 2002001386 A2 Based on WO 2000072022; JP 2003500073 W Based on WO 2000072022; MX 2001011894 A1 Based on WO 2000072022

PRAI DE 1999-19923568 19990521; DE 1999-19923567 19990521

AB WO 200072022 A UPAB: 20040608

NOVELTY - Incorporating **gcpE** and yfgB **genes** into viruses and cells for increasing isoprenoid content and identifying e.g. antimicrobial agents, comprises using DNA sequences (I) from the **gcpE** or yfgB **genes** of **bacteria** or parasites or DNA sequences (II) which hybridize to the specified **genes** or encode a plastid protein with the same biological activity as those encoded by the **genes**.

DETAILED DESCRIPTION - Incorporating **gcpE** and yfgB **genes** into viruses and cells comprises using:

(i) DNA sequences (I) from the **gcpE** or yfgB **genes** of **bacteria** or parasites; or

(ii) DNA sequences (II) which:

(a) hybridize to the specified **genes** or their analogs or derivatives produced by insertion, deletion or substitution; or

(b) encode a plastid protein with the same biological activity as those encoded by the specified **genes**.

INDEPENDENT CLAIMS are also included for the following:

(1) plant cells containing (I) or (II);

(2) transformed plant cells, and transgenic plants regenerated from them, that contain (I) or (II);

(3) determining the enzymatic activity of a **gcpE** protein; or

(4) screening compounds (A) that have antimycotic, antiparasitic or antiviral activity in humans or animals or antiviral, antiparasitic, fungicidal or herbicidal activity in plants.

ACTIVITY - **Antibacterial**; antimycotic; antiparasitic; antiviral; fungicidal; herbicidal. No biological data is given.

MECHANISM OF ACTION - Isoprenoid biosynthesis kinase.

USE - (I) and (II) are used:

(i) to increase the isoprenoid levels in viruses and cells;

(ii) for determining the enzymatic activity of **gcpE** and

yfgB proteins; and
(iii) to identify compounds that **inhibit** activity of **gcpE**, i.e. potential **antibacterial**, antimycotic, antiparasitic or antiviral agents for use in humans or animals, or antiviral, antiparasitic, fungicidal or herbicidal agents for agriculture. Dwg.0/0

L44 ANSWER 33 OF 34 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-422851 [36] WPIX
DNC C2000-127873
TI New isolated **bacterial** signaling factor, useful e.g. for detecting potential **antibacterial** agents, interacts with LuxQ protein to induce expression of a luminescence operon in Vibrio harveyi.
DC B04 B05 D16
IN BASSLER, B; SURETTE, M G; BASSLER, B L
PA (UYPR-N) UNIV PRINCETON; (UYTE-N) UNIV TECHNOLOGIES INT; (UYTE-N) UNIV TECHNOLOGIES INT INC; (BASS-I) BASSLER B L; (SURE-I) SURETTE M G; (USGO) US GOVERNMENT
CYC 88
PI WO 2000032152 A2 20000608 (200036)* EN 196
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 2000019338 A 20000619 (200044)
EP 1135144 A1 20010926 (200157) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
KR 2001093800 A 20011029 (200223)
US 2002072052 A1 20020613 (200243)
US 2002107364 A1 20020808 (200254)#
US 2003096330 A1 20030522 (200336)
US 2003096376 A1 20030522 (200336)
US 2003104606 A1 20030605 (200339)
US 2003148414 A1 20030807 (200358)
US 2003166289 A1 20030904 (200359)
JP 2003526327 W 20030909 (200360) 150
US 2004033548 A1 20040219 (200414)
MX 2001005448 A1 20030401 (200415)
US 6720415 B2 20040413 (200425)
ADT WO 2000032152 A2 WO 1999-US28751 19991202; AU 2000019338 A AU 2000-19338 19991202; EP 1135144 A1 EP 1999-963011 19991202, WO 1999-US28751 19991202; KR 2001093800 A KR 2001-706954 20010602; US 2002072052 A1 Provisional US 1998-110570P 19981202, Div ex US 1999-453976 19991202, US 2001-961452 20010921; US 2002107364 A1 Div ex US 1999-453976 19991202, US 2001-961453 20010921; US 2003096330 A1 Provisional US 1998-110570P 19981202, Div ex US 1999-453976 19991202, US 2001-961507 20010921; US 2003096376 A1 Provisional US 1998-110570P 19981202, Div ex US 1999-453976 19991202, US 2001-961637 20010921; US 2003104606 A1 Provisional US 1998-110570P 19981202, Div ex US 1999-453976 19991202, US 2001-961458 20010921; US 2003148414 A1 Provisional US 1998-110570P 19981202, US 1999-453976 19991202; US 2003166289 A1 Provisional US 1998-110570P 19981202, Div ex US 1999-453976 19991202, Cont of US 2001-961507 20010921, US 2003-409783 20030407; JP 2003526327 W WO 1999-US28751 19991202, JP 2000-584850 19991202; US 2004033548 A1 Provisional US 1998-110570P 19981202, Div ex US 1999-453976 19991202, CIP of US 2001-961507 20010921, US 2003-387345 20030310; MX 2001005448 A1 WO 1999-US28751 19991202, MX 2001-5448

20010531; US 6720415 B2 Provisional US 1998-110570P 19981202, US 1999-453976 19991202

FDT AU 2000019338 A Based on WO 2000032152; EP 1135144 A1 Based on WO 2000032152; JP 2003526327 W Based on WO 2000032152; MX 2001005448 A1 Based on WO 2000032152

PRAI US 1998-110570P 19981202; US 1999-453976 19991202;
US 2001-961452 20010921; US 2001-961453 20010921;
US 2001-961507 20010921; US 2001-961637 20010921;
US 2001-961458 20010921; US 2003-409783 20030407;
US 2003-387345 20030310

AB WO 200032152 A UPAB: 20000801

NOVELTY - An isolated **bacterial** extracellular signaling factor (A) comprising at least one polar, uncharged molecule, having a molecular weight below 1000 kDa, and interacting with LuxQ protein to induce expression of a Vibrio harveyi operon, comprising the luminescence **genes** luxCDABE, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated **bacterial** signaling factor, comprising formula (I) or (II)

(2) an optically active isomer of (II);

(3) method for identifying a compound (III) that regulates activity of a signaling factor (SF), comprising:

(a) contacting SF with (III);

(b) measuring the activity of SF in the presence and absence of (III), and comparing the values; and

(c) identifying a compound regulating the activity of (III);

(4) method for detecting an autoinducer molecule (IV) in a sample, comprising:

(a) contacting the sample with a **bacterial** cell, or extract, comprising biosynthetic pathways that produce light in response to an exogenous autoinducer, the cell has at least two alterations in **gene** loci that participate in autoinducer pathways, the alterations **inhibit** detection of one autoinducer and the production of another; and

(b) measuring the light produced by the cell, or extract;

(5) **bacterial** cell having at least two distinct alterations in **gene** loci involved in autoinducer pathways, the alterations **inhibit** detection of one autoinducer and the production of another;

(6) method for identifying an autoinducer analog (V) that regulates activity of (V), comprising:

(a) contacting a **bacterial** call, or extract, comprising biosynthetic pathways which produces light in response to an autoinducer, with (V); and

(b) comparing the amount of light produced by the cell, or extract, in the presence and absence of (V), a change in the production indicates a (V) which regulates autoinducer activity;

(7) production of autoinducer-2 (IV-2) by reacting S-adenosylhomocysteine (SAH) or S-ribosylhomocysteine (SRH) with a LuxS protein;

(8) production of autoinducer-2, comprising:

(a) contacting SAH with a 5'-methylthioadenosine/S-adenosylhomocysteine nucleosidase (**pfs**) protein, to promote conversion of SAH to SRH; and

(b) contacting SRH with LuxS protein, to promote conversion of SRH to autoinducer-2;

(9) method for detected a (IV)-associated **bacterial** biomarker, comprising:

(a) contacting at least one **bacterial** cell with an autoinducer molecule, to promote induction of a **bacterial** biomarker; and

(b) detecting the **bacterial** biomarker;

(10) method for detecting a target compound (VI) that binds to LuxP protein, comprising contacting the LuxP protein with the target compound, and detecting the binding of the compound to LuxP;

(11) method for regulating formation of **bacterial** biofilm by treatment with a compound that regulates (IV-2) activity, comprising contacting a **bacterium** capable of biofilm formation with a compound capable of regulating biofilm formation, the compound regulates (IV-2) activity;

(12) isolated nucleic acid (VII) that encodes a protein (VIII) necessary for biosynthesis of (A);

(13) a recombinant DNA comprising a vector that contains (VII);

(14) polypeptides produced by expressing (VII);

(15) an isolated nucleic acid (IX) having a 519, 516, or 492 nucleotide sequence, all fully defined in the specification, or a variant or natural mutant of the sequence, a sequence hybridizing with it, or its complement, or a sequence encoding a 172, 171, or 164 residue amino acid sequence, all fully defined in the specification;

(16) a recombinant DNA molecule comprising a vector containing (IX);

(17) a polypeptide produced by expression of (IX);

(18) purifying (A), comprising:

(a) growing bacterial cells that produce (A);

(b) separating the cells from the culture medium;

(c) incubating the cells in a solution having high osmolarity, under conditions promoting production and secretion of protein from the cells;

(d) separating the cells from the solution; and

(e) purifying the factor from the solution;

(19) purified (A) from the method of (18); and

(20) kit comprising the cells of (5).

R1, R2, R3, and R4 = independently e.g. hydrido, halo, alkyl, haloalkyl, cycloalkyl, cycloalkenyl, heterocyclyl, methyl, cyano, alkoxycarbonyl, amino, carboxyl, hydroxyl, formyl, nitro, fluoro, chloro, bromo,aryl, heteroaryl, arakyl, heteroarylalkyl, alkylsulfonyl, hydroxyalkyl, mercaptoalkyl, alkoalkyl, aryloxyalkyl, heteroaryloxyalkyl, aralkyloxyalkyl, heteroarylalkyloxyalkyl, alkylthioalkyl, arylthioalkylphenyl, cyclohexyl, furyl, imidazolyl, pentyl, hexyl, trichloromethyl, dichloropropyl, n-butoxy, methylcarbonyl, ethanoxycarbonylethyl, thienyl, or methylenedioxy.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - (A) regulators.

USE - (A) are used to identify specific regulators which are used to regulate production of bacterial biofilm, and as potential antibacterial agents, e.g. for treating infections in fish caused by V. angufflarum or Aeromonas species. (A) can also be used as bacterial culture additives to stimulate cellular metabolism, growth or repair, e.g. for cultures being used to produce antibiotics. Genes and their derived proteins involved in synthesis of (A) are also useful as therapeutic targets, including for development of vaccines, which may have a broad spectrum of activity since common antigenic determinants may be present in the LuxP and LuxQ proteins. luxS DNA, or its fragments, are useful as probes and primers and for recombinant production of proteins, and which are used to raise antibodies or to produce crystals for structure determination, used in rational drug design.

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AN 2000-639611 [62] WPIX
DNC C2000-192607
TI Essential **genes** from **bacteria**, useful in screening for antimicrobial agents, and related proteins, transformants and antisense sequences.
DC B04 D16
IN BROETZ, H; EHLERT, K; FREIBERG, C; LABISCHINSKI, H; SPALTMANN, F; WIELAND, B
PA (FARB) BAYER AG
CYC 93
PI DE 19916176 A1 20001012 (200062)* 27
WO 2000061792 A1 20001019 (200062) GE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000041119 A 20001114 (200108)
EP 1171629 A1 20020116 (200207) GE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002541819 W 20021210 (200301) 54
ADT DE 19916176 A1 DE 1999-1016176 19990410; WO 2000061792 A1 WO 2000-EP2713 20000328; AU 2000041119 A AU 2000-41119 20000328; EP 1171629 A1 EP 2000-920599 20000328, WO 2000-EP2713 20000328; JP 2002541819 W JP 2000-611714 20000328, WO 2000-EP2713 20000328
FDT AU 2000041119 A Based on WO 2000061792; EP 1171629 A1 Based on WO 2000061792; JP 2002541819 W Based on WO 2000061792
PRAI DE 1999-19916176 19990410
AB DE 19916176 A UPAB: 20001130
NOVELTY - Essential **genes** (I) encoding Escherichia coli proteins (II) designated YQGF, **YHBC**, **YGGJ**, **YGBP**, **YCHB**, **YGBB**, **YJEE** and **KDTB**, and **genes** (Ia) that encode orthologous **gene** products (IIa) in other microorganisms, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) **genes** (III) that include at least a part of (I) or (Ia);

(2) protein products of (I), (Ia) or (III);

(3) a vector containing (I), (Ia) or (III);

(4) transformed microorganisms containing (I), (Ia) or (III);

(5) antisense constructs derived from (I), (Ia) or (III); and

(6) purifying (A) using antibodies.

ACTIVITY - **Antibacterial**. No biological data is given.

MECHANISM OF ACTION - **Inhibiting** expression, or activity, of essential **gene** products.

USE - Recombinant microorganisms in which expression of (I) or (Ia) can be regulated are used to identify compounds that bind to the **gene** products, particularly in affinity selection assays. (II) and (IIa) are used to identify, or prepare, antibodies and other proteins that bind to the **gene** products. Substances that bind to (II) or (IIa) are potentially useful as **antibacterials** for treating a wide range of infections in humans and animals. Sequences antisense to (I) and (Ia) can also be used as **antibacterials**.

ADVANTAGE - The specified **genes** are widely distributed in **bacteria** but have no close homologs in eukaryotic cells.

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